DRUG DETERMINATION POLICY

Title: DDP-27 Allergy and Asthma Specialty Agents

Effective Date: 8/23/23

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of Xolair (omalizumab), Dupixent (dupilumab), Cinqair (reslizumab), Fasenra (benralizumab), Nucala (mepolizumab), Adbry (tralokinumab), and Tezspire (tezepelumab).

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Specialty allergic and asthma agents are specialty drugs indicated for specific diagnoses and are associated with some toxicity. These criteria were developed and implemented to ensure appropriate use of first line conventional therapy as well as use for the appropriate severity of disease.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. General Considerations for Use

A. Appropriate medication use [must meet all listed below]:

1. Diagnosis: meets standard diagnostic criteria that designates signs, symptoms, and test results to support specific diagnosis.

2. Food and Drug Administration (FDA) approval status [must meet one listed below]:

a. FDA approved: product, indication, and/or dosage regimen.

b. Non-FDA approved use: Compendium support (Lexicomp®) for use of a drug for a non-FDA approved indication or dosage regimen.

3. Place in therapy: sequence of therapy supported by national or internationally accepted guidelines and/or studies (e.g., oncologic, infectious conditions).

B. Required site-of-care as determined by the Health Plan (DDP-08 Site of Care for Administration of Parenteral Specialty Drugs).

C. Pharmaceutical sample use: The Plan does not recognize samples as a medication trial or for continuation of therapy.

D. Adherence to requested medication required for re-approval [must meet one listed below]:

1. Medications processed on the medical benefit: consistent utilization (at least 80% of days covered) history documented in claims history or chart notes.

2. Medications processed on the pharmacy benefit: consistent (at least 80% of days covered) fill history electronically or verbally from pharmacy.

E. Exclusion: Concomitant therapy with other biologics or immune modulators.

II. Asthma

A. Moderate to severe persistent allergic asthma [must meet all listed below]:

1. Age: at least six years.

2. Diagnosis and severity [must meet all listed below]:

a. Moderate-severe persistent asthma for over one-year duration.

b. Allergic component [must meet both listed below]:

i. Skin prick: positive immediate responses to at least one allergen (dust mite, cockroach, dog, or cat).

ii. Total Serum IgE: at least 30 to less than or equal to 700 IU/mL.

c. Pulmonary function test (PFT): historical PFT that confirms the diagnosis of asthma.

d. Asthma status: two asthma exacerbations that required treatment with systemic corticosteroids, emergency department visits, or hospitalization for asthma in the last year.

3. Other therapies: A trial of both regimens listed below is required unless contraindicated. Trial must result in an inadequate response or severe adverse reaction:

a. Inhaled corticosteroids (ICS) with long-acting beta-agonist (LABA): three months current use of high dose ICS with LABA and documentation of consistent use.

b. Systemic steroids: intermittent oral or parenteral steroids use to control asthma symptoms.

4. Dosage regimen: this agent is add-on therapy to other asthma medications.

a. Xolair subcutaneous (omalizumab SQ) (see tables in Appendix I).

B. Severe Eosinophilic Asthma.

1. Age:

   a. Cinqair intravenous (reslizumab IV): at least 18 years.

   b. Dupixent subcutaneous (dupilumab SQ): at least six years.

   c. Fasenra subcutaneous (benralizumab SQ): at least 12 years.

   d. Nucala subcutaneous (mepolizumab SQ): at least six years.

2. Diagnosis and severity [must meet one listed below]

   a. Severe Eosinophilic Asthma [must meet all listed below]:

      i. Blood eosinophil count: at least 150 cells/uL at start of treatment OR at least 300 cells/uL in prior 12 months. (Note: 1 microliter [uL] = 1 cubic millimeter [mm^3]).

      ii. Pulmonary function test (PFT): historical PFT that confirms the diagnosis of asthma.

      iii. Asthma Status: two asthma exacerbations that required treatment with systemic corticosteroids or emergency department visits or hospitalization for asthma in the last year.

3. Other therapies: uncontrolled symptoms despite trial of both regimens below with one regimen currently in use:

   a. Six months inhaled corticosteroid (ICS) plus three months long-acting beta agonist (LABA).

   b. Three months ICS plus three months daily oral steroids plus three months LABA.

4. Dosage regimen: these agents are add-on therapy to other asthma medications.

   a. Cinqair intravenous (reslizumab IV): 3mg per kg IV every four weeks.

   b. Dupixent subcutaneous (dupilumab SQ):

Age	Weight	Loading Dose	Maintenance Dose
6 to 11 years*	15 to <30 kg	NA	100mg every other week OR 300mg every four weeks
	≥30 kg	NA	200mg every other week
≥ 12 years to	15 to <30 kg	600 mg once	300 mg every four weeks
	30 to <60 kg	400 mg once	300 mg every two weeks
	≥60 kg	600 mg once	300 mg every two weeks
≥18 years		600 mg once	300 mg every two weeks

   c. Fasenra subcutaneous (benralizumab SQ): 30mg every four weeks for three doses, then every eight weeks.

d. Nucala subcutaneous (mepolizumab SQ):

i. Six to twelve years - 40mg every four weeks.

ii. Over twelve years - 100mg every four weeks.

C. Moderate to Severe Corticosteroid Dependent Asthma

1. Age: at least six years.

2. Diagnosis and severity.

a. Moderate to severe corticosteroid dependent asthma [must meet all listed below]:

i. Required daily oral corticosteroids in addition to regular use of high-dose inhaled corticosteroids plus an additional controller for the past six months.

ii. Pulmonary function test (PFT): historical PFT that confirms a diagnosis of asthma.

3. Other therapies: Combination therapy for the past six months with a high dose inhaled corticosteroid, daily systemic corticosteroids, and either a long-acting beta-agonist (LABA) or a leukotriene receptor antagonist:

a. High-dose inhaled corticosteroids: >500 µg total daily dose of fluticasone propionate or equivalent)

b. Additional asthma controller medication

i. Long-acting beta agonist

ii. Leukotriene receptor antagonist

c. Daily systemic corticosteroids: 5 to 35 mg per day of prednisone or prednisolone or an equivalent

4. Dosage regimen: Dupixent is an add-on therapy to other asthma medications.

a. Dupixent subcutaneous (dupilumab SQ):

Age	Weight	Loading Dose	Maintenance Dose
6 to 11 years*	15 to <30 kg	NA	100mg every other week OR 300mg every four weeks
	≥30 kg	NA	200mg every other week
≥ 12 years to < 18 years	15 to <30 kg	600 mg once	300 mg every four weeks
	30 to <60 kg	400 mg once	300 mg every two weeks
	≥60 kg	600 mg once	300 mg every two weeks
≥18 years		600 mg once	300 mg every two weeks

D. Severe Asthma

1. Age: at least 12 years.

2. Diagnosis and severity [must meet all listed below]:

    a. Severe persistent asthma for over one-year duration.

    b. Asthma Status: persistent symptoms and/or two asthma exacerbations that required treatment with systemic corticosteroids, emergency department visits or hospitalization for asthma in the last year.

3. Other therapies: uncontrolled symptoms despite adherence with maximal optimized therapy and worsening when high dose treatment is decreased.

    a. Inhaled corticosteroids (ICS) with long-acting beta agonist (LABA); three months current use of high dose ICS with LABA and documentation of consistent use.

4. Dosage regimen: Tezspire is an add-on therapy to other asthma medications.

    a. Tezspire subcutaneous (tezepleumab SQ): 210 mg once every four weeks.

E. Approval.

1. Initial: six months.

2. Re-approval: six months to one year [must meet all listed below]:

    a. Adherence to maintenance inhalers: consistent fill history confirmed by claims history or verbally from pharmacy.

    b. Response to medication [must meet one listed below]:

        i. Decreased use of rescue medications.

        ii. Decreased exacerbations.

        iii. Increased forced expiratory volume over 1 minute (FEV1) from pre-treatment baseline.

        iv. Reduced asthma symptoms: coughing, fatigue, SOB, sleep disturbances, or wheezing.

III. Moderate to Severe Chronic Idiopathic Urticaria (CIU) [must meet all listed below]:

A. Age: at least 12 years.

B. Diagnosis and severity: moderate to severe CIU for one year [must meet one listed below]:

1. Urticaria activity score (UAS): at least 28 (see Appendix IV).

C. Other therapies (see Appendix III): Trial of all listed below is required unless contraindicated. Trial must result in an inadequate response (continued hives with itching) or severe adverse reaction:

1. First line: two non-sedating H1 antihistamines for two weeks each.

2. Second line: maximum dose non-sedating H1 antihistamines for one to four weeks.

3. Add to second line: cyclosporine or montelukast for four months.

D. Dosage regimen:

1. Xolair subcutaneous (omalizumab SQ): 150 to 300mg every four weeks (not dependent on serum IgE or weight).

E. Approval.

1. Initial: six months

2. Re-approval: six months to one year; decreased hives (reduction in UAS).

IV. Atopic Dermatitis.

A. Age:

1. Dupixent (dupilumab): at least six months.

2. Adbry (tralokinumab): at least 18 years.

B. Prescriber: dermatologist or allergist.

C. Diagnosis and severity: moderate to severe atopic dermatitis not controlled with topical prescription therapies or if the therapies are not advisable [must meet all listed below]:

1. Exacerbating factors that could contribute to the member's atopic dermatitis have been evaluated and addressed (e.g., non-compliance, environmental triggers, allergy patch testing, etc.).

2. Body surface area (BSA): at least 10 percent.

3. Severity [must meet both below]:

a. Documentation of current pruritus and other symptoms severity (e.g., edema, erythema, erosions. Excoriations, oozing/crusting and/or, lichenification).

b. Interfering with routine daily activities (e.g., skin infections, sleep disturbances).

D. Other therapies: A trial of corticosteroid and one calcineurin inhibitor below is required unless contraindicated. Trial must result in an inadequate response after two consecutive months of use per medication or a severe adverse reaction.

1. Mid-strength to super-potent corticosteroid: unless the face, neck, and/or intertriginous areas are affected.

2. Topical calcineurin Inhibitor: tacrolimus, pimecrolimus.

E. Dosage regimen [must meet one listed below]:

1. Dupixent subcutaneous (dupilumab SQ) [must meet all listed below]:

Age	Weight	Loading Dose	Maintenance Dose
≥ 6 months to ≤ 6 years	5 to <15 kg 15 to <30 kg		200 mg every four weeks
	15 to <30 kg		300 mg every four weeks

≥ 6 years to ≤ 17 years	15 to <30 kg	600 mg once	300 mg every four weeks
	30 to <60 kg	400 mg once	300 mg every two weeks
	≥60 kg	600 mg once	300 mg every two weeks
≥18	Any	600 mg once	300 mg every two weeks

2. Adbry subcutaneous (tralokinumab SQ) [must meet all listed below]:

Age	Weight	Loading Dose	Maintenance Dose
≥18 years	<100 kg	600 mg once	300 mg every two weeks*
	≥100 kg	300 mg once	300 mg every two weeks

* In patients with body weight <100 kg who achieve clear or almost clear skin after 16 weeks of therapy, may reduce dosage to 300 mg every 4 weeks.

F. Approval.

1. Initial: six months.

2. Re-approval: one year [must meet all listed below]:

a. Demonstrate a reduced percentage of body surface area affected, reduced pruritus/symptom severity, and/or improved ability to perform routine daily activities.

b. Adbry Only: evaluate for frequency reduction to every four weeks if <100 kg.

V. Chronic rhinosinusitis with nasal polyps [must meet all listed below]:

A. Age: at least 18 years.

B. Diagnosis and severity [must meet all listed below]:

1. Mucosal inflammation: moderate to severe.

2. Symptoms for at least 12 weeks [must meet two listed below]:

a. Decreased or loss of smell.

b. Nasal obstruction.

c. Mucopurulent rhinorrhea.

d. Facial pressure, pain, fullness.

3. Polyps: confirmed by direct examination, endoscopy, or sinus CT scan.

C. Other therapies: Trials of initial therapies, maintenance therapies, and surgery as listed below are required unless contraindicated. Trial must result in an inadequate response or severe adverse reaction.

1. Initial therapies [must meet both listed below]:

a. Oral corticosteroids for 10 to 15 days within the last two years.

b. Current infection: treated with antibiotics.

2. Maintenance therapies [must meet both listed below]:

a. Intranasal corticosteroids for six months.

b. Anti-leukotrienes plus intranasal corticosteroids for three months.

3. Surgery: primary or revision endoscopic sinus surgery.

D. Dosage regimen:

1. Dupixent Subcutaneous (dupilumab SQ): 300mg every two weeks.

2. Nucala subcutaneous (mepolizumab SQ): 100mg every four weeks.

E. Approval:

1. Initial: six months.

2. Re-approval: six months to one year; reduction of symptoms as well as number and/or size of polyps.

VI. Eosinophilic granulomatosis with polyangiitis [must meet all listed below]:

A. Diagnosis and severity [must meet all listed below]:

1. Diagnostic criteria [must meet four of the six listed below]:

a. Asthma.

b. Eosinophilia: above ten percent on differential white blood cell count.

c. Mononeuropathy or polyneuropathy.

d. Migratory or transient pulmonary opacities detected radiographically.

e. Paranasal sinus abnormality.

f. Biopsy containing a blood vessel showing the accumulation of eosinophils in extravascular areas.

2. Labs: eosinophilia (above 500/uL) or hypereosinophilia (above 1,500/uL).

3. Severity:

a. Five-factor score: 1 (see Appendix II).

B. Other therapies: Trials of one systemic steroid, cyclophosphamide, and one disease-modifying agent listed below are required unless contraindicated. Trial must result in an inadequate response or severe adverse reaction.

1. Systemic corticosteroids: treat until manifestation of disease is controlled and taper over approximately 12 to 18 months [must meet one listed below]:

a. Systemic vasculitis: prednisone 0.5-1 mg per kg.

b. Acute multi-organ disease: methylprednisolone 1 g daily for three days followed by oral therapy.

2. Cyclophosphamide [must meet both listed below]:

    a. Five-factor score: 2 or 1 (see Appendix II) with cardiac or central nervous system involvement.

    b. Use corticosteroids concomitantly.

3. Maintenance therapy.

    a. Disease-modifying agents: azathioprine, methotrexate, leflunomide.

C. Dosage regimen: [must meet both listed below]:

1. Nucala subcutaneous (meplizumab SQ): 300mg every four weeks.

2. Concomitant drugs: corticosteroids.

D. Approval:

1. Initial: six months.

2. Reapproval: one year; Reduced eosinophil count and steroid dose.

VII. Hypereosinophilic syndrome.

A. Age: at least 12 years.

B. Diagnosis and severity [must meet all listed below]:

1. Diagnosis [must meet both listed below]:

    a. Non-myeloid disease with T cell lymphocytic variant or idiopathic.

    b. IgE level: at or above 1,500 eosinophils per mm^3

2. Severity.

    a. Symptomatic patients or those with evidence of end-organ damage.

C. Other therapies: Trials of corticosteroids and hydroxyurea as listed below are required unless all are contraindicated. Trial must result in an inadequate or severe adverse reaction.

1. Corticosteroids: prednisone 20 to 60mg daily depending on the severity of disease manifestations and eosinophilia presence; titrate to response.

2. Hydroxyurea: 500 to 1000mg per day, titrated to 2000mg per day as tolerated [must meet one below]:

    a. Add on to corticosteroids if steroid toxicity has become dose limiting.

    b. Monotherapy for corticosteroid-resistant patients.

D. Dosage regimen:

1. Nucala subcutaneous (mepolizumab SQ): 300mg every four weeks.

2. Concomitant administration with corticosteroids.

E. Approval

1. Initial: six months.

2. Re-approval: one year; decreased or sustained reduction in disease activity.

VIII. Eosinophilic Esophagitis

A. Age: at least 12 years.

B. Weight: at least 40 kg.

C. Prescribed by or in consultation with an allergist or gastroenterologist.

D. Diagnosis and Severity

1. Endoscopic biopsy with a peak eosinophil count of at least 15 per high-powered field or 60 eosinophils per mm^2

2. Secondary causes of esophageal eosinophilia have been ruled out (gastroesophageal reflux disorder, hypereosinophilic syndrome, Crohn's disease with esophageal involvement, etc.)

3. Symptoms related to esophageal dysfunction are present (dysphagia, food impaction, chest pain, heartburn, etc.)

E. Other Therapies: Trial of one proton pump inhibitor and one topical corticosteroid listed below is required unless all are contraindicated. Trial must result in an inadequate response after two consecutive months of use per medication or severe adverse reaction.

1. Proton Pump Inhibitor: dosed twice daily.

2. Swallowed Topical Corticosteroids: Budesonide inhalation solution swallowed as a viscous slurry, fluticasone propionate administered by mouth via metered dose inhaler and swallowed.

F. Dosage Regimen

1. Dupixent Subcutaneous (dupilumab SQ): 300mg every week.

G. Approval

1. Initial: six months.

2. Re-approval: one year; decreased or sustained reduction in disease activity

4.0 Coding:

COVERED CODES				
Code	**Brand Name**	**Generic Name**	**Billing (1 unit)**	**Prior Approval**
J2357	Xolair	omalizumab	5mg	Y
J2182	Nucala	mepolizumab	1mg	Y

COVERED CODES				
Code	**Brand Name**	**Generic Name**	**Billing (1 unit)**	**Prior Approval**
J2786	Cinqair	reslizumab	1mg	Y
J0517	Fasenra	benralizumab	1mg	Y
J2356	Tezspire	tezepelumab	1 mg	Y

EXCLUDED CODES			
Code	**Brand Name**	**Generic Name**	**Benefit Plan Reference/Reason**
J3590	Dupixent	dupilumab	Covered on the pharmacy benefit with prior approval
NA	Adbry	tralokinumab	Covered on the pharmacy benefit with prior approval

Medication	**Process through pharmacy benefit**	**Process through medical benefit**
Adbry	Prefilled syringe	*(none)*
Cinqair	*(none)*	Vial
Dupixent	Pre-filled syringe Pen injector	*(none)*
Fasenra	Pen auto-injector Pre-filled syringe (HCP administration only)	Pre-filled syringe (HCP administration only)
Nucala	Auto-injector Syringe	Vial
Tezspire	(none)	Pre-filled syringe (HCP administration only)
Xolair	Pre-filled Syringe	Vial

**HCP = health care professional*

5.0 References, Citations & Resources:

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6.0 Appendices:

See pages 14-18.

7.0 Revision History:

Original Effective Date: 05/03/2004

Next Review Date: 11/10/2023

Revision Date	Reason for Revision
7/19	Moved to new format
9/19	Replaced abbreviations, added Dupixent, added diagnosis of chronic rhinosinusitis with polys, clarified dosage, reformatted approval sections
10/20	Annual review: clarify criteria instructions, revised Xolair/Nucala/Dupixent age, indicated add-on treatment for asthma, revised other therapies language, updated Xolair dosage table, changed Fasenra J code; replaced abbreviations, added exclusion of use in non-FDA approved indications, clarified Dupixent dosing, formatting, approved by P&T Committee 12/9/20
2/21	Off cycle review, added diagnoses eosinophilic granulomatosis with polyangiitis and hyperesosinophilic syndrome; replaced abbreviation, clarified criteria instructions
10/21	Annual review: added Nucala for rhinosinusitis with nasal polyps, added diagnosis Atopic dermatitis, removed NCCN reference under appropriate use
6/22	Ad Hoc review; addition of Atopic Dermatitis indication, addition of GINA guidelines in references
6/23	Off cycle review: fixed formatting, added severe asthma (Tezspire), Eosinophilic esophagitis, added general considerations for use section: adherence requirement, site of care, no sample use, no concomitant use with other biologics or immune modulators. Changed title to Allergy and Asthma Specialty Agents for website alpha look.

Appendix I: Adult and Pediatric Xolair Dosing

Adult and adolescent patients 12 years of age and older: Initiate dosing according to Table 1.

Table 1. Subcutaneous XOLAIR Doses Every 2 or 4 Weeks* for Patients 12 Years of Age and Older with Asthma

Pretreatment Serum IgE (IU/mL)	Dosing Freq.	Body Weight			
		30–60 kg	>60–70 kg	>70–90 kg	>90–150 kg
		Dose (mg)			
≥30–100	Every 4 weeks	150	150	150	300
>100–200		300	300	300	225
>200–300		300	225	225	300
>300–400	Every 2 weeks	225	225	300	Insufficient Data to Recommend a Dose
>400–500		300	300	375	
>500–600		300	375	Insufficient Data to Recommend a Dose	
>600–700		375	Insufficient Data to Recommend a Dose		

*Dosing frequency:

- Subcutaneous doses to be administered every 4 weeks
- Subcutaneous doses to be administered every 2 weeks

Table 2. Subcutaneous XOLAIR Doses Every 2 or 4 Weeks* for Pediatric Patients with Asthma Who Begin XOLAIR Between the Ages of 6 to <12 Years

Pre-treatment Serum IgE (IU/mL)	Dosing Freq.	Body Weight									
		20-25 kg	>25-30 kg	>30-40 kg	>40-50 kg	>50-60 kg	>60-70 kg	>70-80 kg	>80-90 kg	>90-125 kg	>125-150 kg
		Dose (mg)									
30-100	Every 4 weeks	75	75	75	150	150	150	150	150	300	300
>100-200		150	150	150	300	300	300	300	300	225	300
>200-300		150	150	225	300	300	225	225	225	300	375
>300-400		225	225	300	225	225	225	300	300	Insufficient Data to Recommend a Dose	
>400-500		225	300	225	225	300	300	375	375		
>500-600		300	300	225	300	300	375	Insufficient Data to Recommend a Dose			
>600-700		300	225	225	300	375	Insufficient Data to Recommend a Dose				
>700-800	Every 2 weeks	225	225	300	375	Insufficient Data to Recommend a Dose					
>800-900		225	225	300	375						
>900-1000		225	300	375	Insufficient Data to Recommend a Dose						
>1000-1100		225	300	375							
>1100-1200		300	300	Insufficient Data to Recommend a Dose							
>1200-1300		300	375								

*Dosing frequency:

- Subcutaneous doses to be administered every 4 weeks
- Subcutaneous doses to be administered every 2 weeks

Appendix II Five-factor score in eosinophilic granulomatosis with polyangiitis (Churg-Strauss)

- Age above 65
- Cardiac insufficiency
- Renal insufficiency (stabilized peak creatinine 1.7mg/dL
- Gastrointestinal involvement
- Absence of ear, nose and throat manifestations (presence is associated with a better prognosis)

Scoring: The presence of each factor is given one point. The five factor score ranges from 0 to 2; a score of 0 is given when none of the factors are present. A score of 1 for one factor, and a score of 2 for two or more factors.

Appendix III: Monitoring & Patient Safety

Drug	Adverse Reactions	Monitoring	REMS
Xolair omalizumab SQ	• Dermatology: injection site reactions (45%; severe – 12%) pregnancy: IgG monoclonal antibodies expected to cross placenta in 3rd trimester	• Asthma Severity: forced expiatory volume (FEV_1), peak flow and/or pulmonary function tests (PFT) • Injection Site Reaction: monitor post infusion (most occur ≤1 hour) • Infections: signs and symptoms	Med Guide: Dispensed w drug
Nucala mepolizumab SQ	• Central Nervous System: headache (19%) • Pregnancy: IgG monoclonal antibodies expected to cross placenta in 3rd trimester	• Asthma Severity: FEV_1, peak flow and/or PFT, use of beta agonist	Not needed
Cinqair reslizumab IV	• Musculoskeletal (MSK): increased creatinine, phosphokinase (20% transient) • Pregnancy: IgG monoclonal antibodies expected to cross placenta in third trimester	• Anaphylaxis: during and post infusion • Asthma Severity: FEV_1, peak flow and/or PFT • Infection: signs and symptoms	Not needed
Fasenra benralizumab SQ	• Immunological: antibody development (12-13%) • Pregnancy: IgG monoclonal antibodies expected to cross placenta in third trimester	• Anaphylaxis: during and post infusion • Asthma Severity: FEV_1, peak flow and/or PFT • Infection: signs and symptoms	Not needed
Dupixent dupilumab SQ	• Local: injection site reaction (10%) • Ophthalmology: conjunctivitis (10%)	• Asthma Severity: PFT • Hypersensitivity • Ophthalmology: ocular effects	None needed
Adbry tralokinumab SQ	• Respiratory: Upper respiratory tract infection (24%) Ophthalmic: Conjunctivitis (6% to 9%)	• Signs and symptoms of hypersensitivity and ocular adverse effects.	Not needed

Appendix III: Recommended Treatment Algorithm for Chronic Urticaria

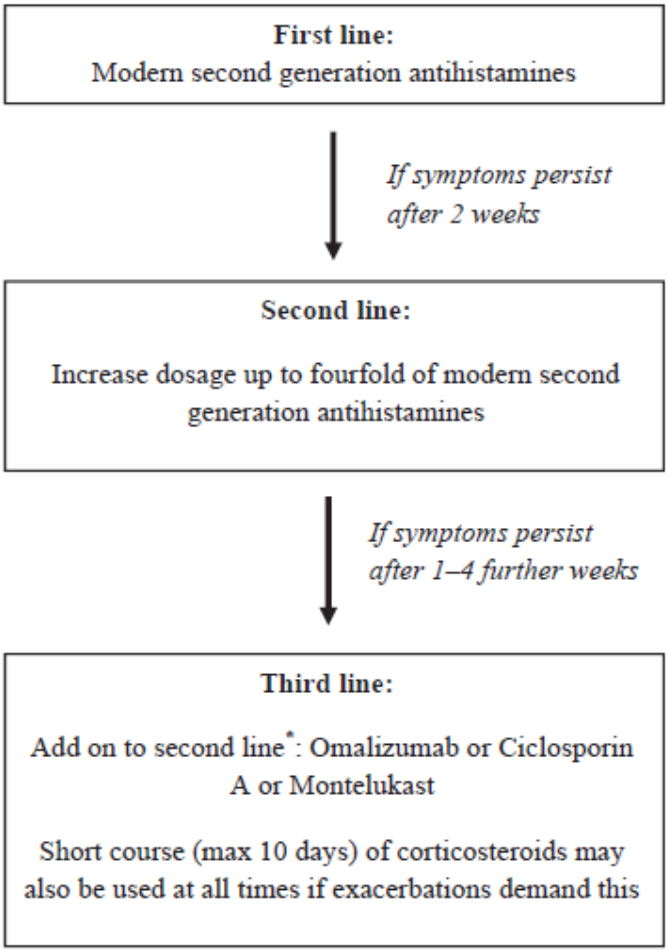

Figure 2 Recommended treatment algorithm for urticaria. *The order of third-line treatments does not reflect preference. *First line = High-quality evidence:* Low cost and worldwide availability (e.g., modern second-generation antihistamines exist also in developing countries mostly cheaper than old sedating Antihistamines), per daily dose as the half-life time is much longer, very good safety profile, good efficacy. *Second line = high-quality evidence:* Low cost, good safety profile, good efficacy. *Third line as add-on to AH. Ciclosporin A = High-quality evidence:* Medium to high cost, moderate safety profile, good efficacy. *Omalizumab = High-quality evidence:* High cost, very good safety profile, very good efficacy. *Montelukast = Low quality evidence:* Low cost, good safety, low efficacy. *Short course of corticosteroids = Low quality evidence:* Low cost, worldwide availability, good safety profile (for short course only), good efficacy during intake, but very low for lasting efficacy.

EAACI/GA²LEN/EDF/WAO guidelines for the definition, classification, diagnosis and management of urticarial: the 2013 revision and update. Allergy 2014:69(7):868-887

Appendix IV: The Urticaria Activity Score (UAS)

The Urticaria Activity Score (UAS) is a composite score of itch severity and hive count

To assess disease severity in patients with chronic idiopathic urticaria (CIU), patients record the severity of their itch and the number of hives 2 times per day (AM AND PM)

Each component of the UAS is scored on a scale of 0 to 3; the 2 scores are added together for a daily total of 0 to 6

Daily scoring the urticaria activity score (UAS)

Score	Itch Severity	Number of Hives
0	None	None
1	Mild	1-6
2	Moderate	7-12
3	Severe	>12

The UAS7 is the sum of the average daily UAS over 7 days

After 7 days, average daily scores from the morning and evening assessments are added together

Values can range between 0 to 21 for weekly itch severity, and 0 to 21 for weekly hive count

The UAS7 ranges from 0 to 42

Appendix V: FDA Approved Indications

Indication	Adbry		Cinqair		Dupixent		Fasenra		Nucala		Tezspire		Xolair	
	A	P	A	P	A	P	A	P	A	P	A	P	A	P
Asthma - Severe Asthma											x	x		
Asthma - Moderate to Severe Corticosteroid Dependent Asthma					x	x								
Asthma - Moderate Eosinophilic Asthma					x	x								
Asthma - Severe Eosinophilic Asthma			x		x	x	x	x	x	x				
Asthma - Moderate to Severe Persistent Allergic Asthma													x	x
Atopic dermatitis	x				x	x								
Chronic Rhinosinusitis with Nasal Polyposis					x								x	
Chronic Spontaneous Urticaria													x	x
Eosinophilic Esophagitis					x	x								
Eosinophilic granulomatosis with polyangiitis														
Hypereosinophilic syndrome														
Prurigo Nodularis					x									

**A = Adult, P = Pediatric*